



58. (New) A method for producing a protein from an endogenous cellular gene comprising:

- (1) introducing a vector comprising a transcriptional regulatory sequence into a cell;
- (2) maintaining said cell under conditions appropriate for integrating said vector into the genome of said cell by non-homologous recombination whereby said transcriptional regulatory sequence is operably linked to said endogenous cellular gene;
- (3) maintaining said cell under conditions appropriate for expressing said endogenous cellular gene in said cell by means of said transcriptional regulatory sequence;
- (4) maintaining said cell so as to produce amounts of said protein from said endogenous cellular gene; and
- (5) purifying said protein.

59. (New) A method for producing a protein from an endogenous cellular gene comprising:

- (1) introducing a vector comprising a non-retrovirus transcriptional regulatory sequence into said cell;
- (2) maintaining said cell under conditions appropriate for integrating said vector into the genome of said cell by non-homologous recombination whereby said transcriptional regulatory sequence is operably linked to said endogenous cellular gene;
- (3) maintaining said cell under conditions appropriate for expressing said endogenous cellular gene in said cell by means of said transcriptional regulatory sequence; and

(4) maintaining said cell so as to produce amounts of said protein from said endogenous cellular gene.

60. (New) A method for producing an expression product of an endogenous cellular gene comprising:

(1) introducing a vector comprising a transcriptional regulatory sequence operably linked to a secretion signal sequence into a cell;

(2) maintaining said cell under conditions appropriate for integrating said vector into the genome of said cell by non-homologous recombination whereby said transcriptional regulatory sequence and secretion signal sequence are operably linked to said endogenous cellular gene;

(3) maintaining said cell under conditions appropriate for expressing said endogenous cellular gene in said cell by means of said transcriptional regulatory sequence; and

(4) maintaining said cell so as to produce amounts of the expression product of said endogenous cellular gene.

61. (New) The method of claim 60 wherein said vector further comprises an unpaired splice donor sequence operably linked to said transcriptional regulatory sequence.

62. (New) The method of claim 60 wherein said transcriptional regulatory sequence is non-retroviral.

63. (New) A method for producing a protein from an endogenous cellular gene comprising:

(1) introducing a vector construct comprising a transcriptional regulatory sequence operably linked to an unpaired splice donor sequence into a cell;

(2) maintaining said cell under conditions appropriate for integrating said vector construct into the genome of said cell by non-homologous recombination whereby said transcriptional regulatory sequence and unpaired splice donor sequence are operably linked to said endogenous cellular gene;

(3) maintaining said cell under conditions appropriate for expressing said endogenous cellular gene in said cell by means of said transcriptional regulatory sequence; and

(4) maintaining said cell so as to produce amounts of the protein encoded by said endogenous cellular gene.

64. (New) The method of claim 63 wherein said transcriptional regulatory sequence is non-retroviral.

65. (New) A method to express and screen for expression of a cellular gene comprising:

(1) introducing a vector construct into a cell and maintaining said cell under conditions appropriate for integrating said vector construct into the genome of a cell, said vector construct lacking targeting sequences and containing a transcriptional regulatory sequence and unpaired splice donor sequence, so that the coding region of a gene in the genome is operably

linked to the transcriptional regulatory sequence and splice donor sequence on the vector construct; and

(2) screening said cell for expression of a protein that is encoded by said gene.

66. (New) The method of claim 65 wherein said transcriptional regulatory sequence is non-retroviral.

67. (New) The method of claim 65 with the additional step of isolating the cell producing the protein encoded by said gene.

68. (New) A method to express and screen for expression of a cellular gene comprising:

(1) introducing a vector construct into a cell and maintaining said cell under conditions appropriate for integrating said vector construct into the genome of a cell by non-homologous recombination, said vector construct containing a transcriptional regulatory sequence and unpaired splice donor sequence, so that the coding region of a gene in the genome is operably linked to the transcriptional regulatory sequence and splice donor sequence on the vector construct; and

(2) screening said cell for expression of a protein encoded by the cellular gene, said gene and said upstream region of said gene lacking homology to the vector construct that would facilitate homologous recombination of the vector construct with the genome to cause expression of said gene.

69. (New) A method to express and screen for expression of a desired phenotype in a cell comprising the steps of:

- (1) constructing a vector comprising a transcriptional regulatory sequence and an unpaired splice donor sequence;
- (2) delivering copies of the vector to a plurality of cells;
- (3) maintaining the cells under conditions permitting non-homologous recombination between the vector and the genome of the cells, thereby expressing an endogenous gene conferring said desired phenotype; and
- (4) screening the non-homologously recombinant cells by assay for the desired phenotype to identify cells in which expression of the desired phenotype occurs.

70. (New) A method as claimed in claim 69 wherein the desired phenotype is production of a particular protein and the assay is conducted by testing for increased production of the protein.

71. (New) A method to express and screen for expression of a desired gene in a cell comprising the steps of:

- (1) constructing a vector comprising a transcriptional regulatory sequence and an unpaired splice donor sequence;
- (2) introducing said vector into at least 100,000 cells;

(3) maintaining said cells under conditions appropriate for integrating the vector by non-homologous recombination into said cells;

(4) screening the non-homologously recombinant cells produced in (3) by assay for a phenotype to identify cells in which the expression of the desired gene has been expressed.

72. (New) A purified cell expressing a protein, said cell comprising in its genome an inserted genetic construct, the genetic construct comprising a transcriptional regulatory sequence operably linked to a splice donor sequence, said transcriptional regulatory sequence being linked effectively in the cell's genome to a gene in the genome encoding said protein so as to cause expression of said gene and said splice donor sequence being spliced to a splice acceptor sequence in said gene, the construct inserted into said gene or upstream region of said gene, said gene and upstream region having no homology to any sequences in the genetic construct that would facilitate homologous recombination of the construct with the genome to cause expression of said gene.

73. (New) The cell of claim 72 wherein the inserted genetic construct additionally contains an amplifiable marker.

74. (New) A purified cell expressing a protein, said cell comprising in its genome an inserted genetic construct, the genetic construct comprising a transcriptional regulatory sequence operably linked to a splice donor sequence, said transcriptional regulatory sequence on the construct being linked effectively in the cell's genome to a gene in the genome encoding said protein so as to cause expression of said gene and said splice donor sequence being spliced to a splice acceptor sequence in said gene, the construct containing no homology to any sequences in said gene or to upstream regions of said gene that would facilitate homologous recombination of the construct with the genome to cause expression of said gene.

75. (New) A method to express and screen for expression of a gene encoding a protein comprising:

- (1) constructing a vector comprising a transcriptional regulatory sequence and an unpaired splice donor sequence;
- (2) introducing said vector into a cell;
- (3) maintaining the cell under conditions permitting non-homologous recombination events between the inserted vector and the genome of the cell whereby said transcriptional regulatory sequence and splice donor sequence are operably linked to said gene; and
- (4) screening the recombinant cell by assay for expression of the protein encoded by said gene, said gene and upstream region of said gene having no homology to the vector that would facilitate homologous recombination of the vector with the genome to cause expression.

76. (New) A purified cell expressing a protein encoded by an endogenous gene, said cell comprising in its genome an inserted genetic construct, the genetic construct comprising a transcriptional regulatory sequence operably linked to a splice donor sequence, said transcriptional regulatory sequence on the construct being linked effectively in the cell's genome to cause expression of a protein encoded by said gene and said splice donor sequence being spliced to a splice acceptor sequence in said gene, the genetic construct being inserted into said gene or upstream region of said gene by non-homologous recombination.

77. (New) A purified cell expressing a protein encoded by an endogenous gene, said cell comprising in its genome an inserted genetic construct, the genetic construct comprising a transcriptional regulatory sequence operably linked to a splice donor sequence, said transcriptional regulatory sequence on the genetic construct being linked effectively in the cell's genome to cause expression of a protein encoded by said gene and said splice donor sequence being spliced to a splice acceptor sequence in said gene, said genetic construct not containing a targeting sequence that would facilitate homologous recombination of the construct with the genome to activate expression of said gene.